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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/937,834	02/13/2002	Johannes Booij	246152015300	5546

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EXAMINER	
BERCH, MARK L	

ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 06/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/937,834	BOOIJ ET AL.	
	Examin r	Art Unit	
	Mark L. Berch	1624	

-- Th MAILING DATE of this communication appears on the c ver sh et with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 May 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10,12-14,16-20,27-29,31,32,34-37,39-44 and 46-54* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10,12-14,16-20,27-29,31,32,34-37,39-44 and 46-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/10/04 has been entered.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 10, 12-14, 16-20, 27-29, 31-32, 34-37, 39-44, 46-54 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "randomly-ordered" is indefinite. This is an especially serious problem because this term is exactly what applicants repeatedly cite as the limitation which distinguishes the claims from the prior art. The core problem is that "random" and "ordered" are essentially opposites of each other. As evidence of this fact, there is cited <http://adams.allwords.com/word-random.html> Allwords.com entry for "random"

which says, "1. Lacking a definite plan, system or order". The Iturriaga reference says, "randomness means unpredictability or lack of order." In Dickakian, see second paragraph of column 1, which refers to "an unordered or random isotropic structure". In Bulst, see first full paragraph of column 3, which says, "a completely unordered distribution of the interruptions is provided, i.e. a mathematical random distribution is present.". In Brand, see column 1 lines 48-49, which says "the alloy particles, which are first present as an unordered or random alloy". These all provide evidence that random and ordered are opposites. Thus, there is no way of determining what this means.

An extremely similar term appears in the specification on page 11 as follows: "The agglomerates of the present invention are not of the rosette type: they consist of small crystals clustered together in a random order (see the Figure)." It is presumed that this is the basis for the similar term currently added to the claims. But this gives no real guidance as to what the term means. Indeed, the use of the term "clustered together" simply makes matters worse, since clustering is a type of non-randomness. The reference to the figure is of no real value. First, it's just an example; it doesn't give us general guidance as to the full scope of the term. And second, its too indistinct to say much of anything. This page 11 mention is the only place that the term (or something seemly equivalent) appears in the specification. In the rest of the places, the term used to distinguish these materials from those of the prior art is "agglomerate", a term not present in the claims.

The sole clue that the claim provides is the proviso present: "with the proviso that the rosette-like crystalline form of Potassium clavulanate is excluded." This tells us that the rosette-like crystalline form is an example of "randomly-ordered" (otherwise the

proviso would not be needed). However, merely knowing one example of "randomly-ordered" is not enough to tell us what the boundaries are for this term. One of ordinary skill in the art cannot tell where the line is between things which are "randomly-ordered" and things which are not. It is possible that the "random" is a relative term, that is, permitting a certain amount of order - - perhaps enough to form the cluster that the specification refers to. If so, note that terms of degree are indefinite when the specification contains no "explicit guidelines" to distinguish from things which are not so, *Ex parte Oetiker*, 23 USPQ2d 1651, 1655 (1990) and *Ex parte Oetiker*, 23 USPQ2d 1641, and *Seattle Box Co. v. Industrial Crating & Packaging, Inc.* 221 USPQ 568, 574. See also *Ex Parte Anderson*, 21 USPQ2d 1241 at 1250.

Two references were supplied, but neither defines the terms and indeed, neither mentions it.

The examiner notes that "randomly ordered" does have an idiomatic meaning, denoting, approximately, out of sequence, or, alternatively, in no sequence at all. Thus, if cards where well-shuffled, they would be randomly ordered. Such a notion would make no sense for crystals, which are not individually labeled and thus could not be said to be out of sequence.

Claims 31, 37, 39-44, and 46-52 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The insertion of "Carr index" is clearly new matter. There is nothing in MPEP §2163.07 to support this. If this were the sole measure of compressibility, it would not be new matter, but there are a number of different measures because there are different ways to measure compressibility. It can be measured under isostatic, uniaxial or multiaxial compaction. Other standards include MPIF Standard 45, ASTM B 331, and, on a more fundamental level, the bulk modulus.

Claims 10-14, 16-20, 25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 10, 12-14, 16-20, 53-54 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for Potassium clavulanate, does not reasonably provide enablement for alkali metal clavulanates. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The claims as written say that <u>any</u> alkali metal clavulanate can be made into a "randomly-ordered" crystalline form from any solvent by adding an anti-solvent solvent The fact that this procedure works with the Potassium clavulanate is no assurance that this will work with different compounds. This is particularly true when dealing with molecules of very different sizes, since size is so often a major factor in crystallization. The Lithium atom is much smaller than potassium, and cesium is much larger than potassium, and thus there is no reason to expect the same crystallization behavior.

Claims 10, 12-14, 16-20, 27-29, 31-32, 34-37, 39-44, 46-54 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The removal of dependency on claim 1 has broadened the claims. The previous limitation of "high water affinity", whatever that meant, has been removed, so that applicants are now covering compounds and crystalline forms thereof which are e.g. not hydroscopic at all. This is beyond (broader than) what the specification teaches is the invention (see page 5, lines 3-6).

The traverse is unpersuasive, and indeed is not entirely understood. Applicants do not dispute that the "high water affinity" limitation has been removed, but point instead to the "agglomerates of randomly ordered clusters" claim language. It is not seen how this helps. Apparently, the "agglomerates of randomly ordered clusters" claim language will accomplish the "high water affinity" requirement, but applicants present no reasoning why this would be so.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 37, 40-42, 44, 46-52 are rejected under 35 U.S.C. 102(b) as being anticipated by USP 4454069, 6417352, or 5288861.

In 4454069, see column 5, lines 36-39, which refers to Potassium clavulanate in the form of "microcrystals ... well-defined needles or waisted plates. 6417352 gives another crystallization. The form is not stated, but conditions which would be expected to obtain the rosettes were not used. In 5288861, a description of different forms appears at column 1, lines 41-45. For particle size, see column 11, lines 16-40, which discloses the distribution of particle size for conventional needles, which are of course hygroscopic. It can be seen that the average size is somewhere in the 640-1280 range for both samples A and B, meaning that claim 44 but not 43 is anticipated.

The traverse is unpersuasive. Applicants earlier argued that these e.g. needles are not agglomerates. But that is a very broad term. It simply means a collection or mass, which could be a collection or mass of needles. Indeed, crystals are agglomerates by their very nature. Second, applicants also argued that the needles of 4454069 have a density of 0.18. However, a) applicants present no evidence that this is true and 2) the 0.18 would be covered by the "about 0.2". The same is true for the compressibility.

With regard to 5288861 and 6417352, it is correct that the references are silent on the matter of its e.g. density characteristic, and 4454069 is silent on the particle size characteristic. However, if mere silence were enough, then every anticipation could be overcome by simply putting in some limitation that the reference happened to be silent about, even if the material were exactly the same as the prior art. One could put in a limitation about density, color, melting point, solubility in some obscure solvent, spectroscopic data, and then simply point to the silence of the reference, as applicants have done here. Applicants could insert the limitation "which does not explode upon tapping" and point out the reference says nothing about this limitation at all.

MPEP 2112 states: "A REJECTION UNDER 35 U.S.C. 102/103 CAN BE MADE WHEN THE PRIOR ART PRODUCT SEEMS TO BE IDENTICAL EXCEPT THAT THE PRIOR ART IS SILENT AS TO AN INHERENT CHARACTERISTIC"

The section goes on as follows:

> "Where applicant claims a composition in terms of a function, property or characteristic and the composition of the prior art is the same as that of the claim but the function is not explicitly disclosed by the reference, the examiner may make a rejection under both 35 U.S.C. 102 and 103, expressed as a 102/103 rejection. "There is nothing inconsistent in concurrent rejections for obviousness under 35 U.S.C. 103 and for anticipation under 35 U.S.C. 102." In re Best, 562 F.2d 1252, 1255 n.4, 195 USPQ 430, 433 n.4 (CCPA 1977). This same rationale should also apply to product, apparatus, and process claims claimed in terms of function, property or characteristic. Therefore, a 35 U.S.C. 102/103 rejection is appropriate for these types of claims as well as for composition claims."

Here, the "function is not explicitly disclosed by the reference" is the compressibility, etc. Applicants need to show that such is not actually present in the reference.

The most recent traverse is also not persuasive. Applicants argue that "agglomerates of randomly ordered crystals" is inconsistent with the references which teach "well-defined needles or plates, or rosette forms." As is noted above, the "randomly ordered" is indefinite and thus cannot be relied upon to distinguish over the prior art. It is not clear moreover why applicants believe that this claim language excludes things which are "well defined" or whether it excludes things which are needles or plates, or possibly both. However, the examiner must note that 5288861 at column 1, line 43-45 has "crystals ... randomly aggregated into loosely formed bundles". Although this is not exactly the same as "randomly ordered crystal agglomerates", it seems fairly close. Aggregated and agglomerates seem to denote about the same thing. While

"ordered" is not present, as noted, it is not clear what this would mean. Perhaps bundles represents a form of ordering.

Claims 37, 39-44, 46-52 are rejected under 35 U.S.C. 102(b) as being anticipated by WO97/33564.

In WO97/33564, see the agglomerate at page 10, lines 13-23, and examples 7-11. Other particle size distributions appear at page 5-6. Potassium clavulanate in crystalline form may be presumed, since it is generally available in that form. Page 10 says, "Mixtures of agglomerates of a p-lactam antibiotic such as amoxicillin trihydrate with a second pharmaceutically active agent, e.g. potassium clavulanate...." Examples 7-11 all have Potassium clavulanate in the agglomerate. The traverse is unpersuasive. Much the same reasoning applies here.

Claims 10, 12-14, 16-19, 27-29, 31-32, 37, 42-44, 51-54 are rejected under 35 U.S.C. 102(b) as being anticipated by Harbridge, Cardoso, WO 98/21212.

The lifting of the requirement for being highly hygroscopic broadens the claims (see description requirement rejection below). Thus, examples such as 18 or 20-21 of Harbridge now anticipate. In Cardoso, see, example 5. In WO 98/21212, see examples 5, 7. Many more references could be cited. There are no process parameters which distinguish the claimed process and that of the prior art, only an alleged difference in the form. The traverse is unpersuasive. Much the same reasoning applies here. Also, in discussing WO 98/21212, applicants note that the prior art needles have a compressibility of 50%, as seen by the fact that their replication of example 6 of the prior art as done on page 17, lines 4-10 gives such a value. Claim 31 has "about 40%". However, the two processes were a little different. In the prior art, the initial clavulanate

suspension was chilled to 12°C, then the K salt was added, and a second cooling was done to 5°C, after the addition was complete. In the replication in the specification, the initial clavulanate suspension was not chilled at all, but instead the K solution was chilled, and added to the unchilled and much larger clavulanate solution. As a result, the final solution would have been somewhere between the 5-10°C of the chilled K solution, and the room temp suspension, but much closer to the latter, since the latter was more than 2 times larger.

Applicants also argue with regard to 98/21212, "Contrary to the Examiner's assertions, the formation of potassium salt in solution alone does not meet the claim language, because the potassium clavulanate solution is not contacted with another portion of anti-solvent." Applicants reading of the claim is not agreed with. The claim does not forbid the K salt from being prepared in situ from the amine; the instant it is formed, the K salt is there in the solvent. As more K 2-ethylhexanoate is added, that is the "another portion of anti-solvent" that the remarks refer to. That is, in terms of the claim language, the "solution or suspension of alkali metal clavulanate" (claim 10) is the Potassium clavulanate formed in situ in what is aqueous acetone. The antisolvent is the additional acetone added. Thus, the first solvent is the water in the aqueous acetone; the antisolvent is acetone.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, THIS ACTION IS MADE FINAL even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37

CFR 1.136(a). A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark L. Berch whose telephone number is 571-272-0663. The examiner can normally be reached on M-F 7:15 - 3:45.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mukund Shah can be reached on (571)272-0674. If you are unable to reach Dr. Shah within a 24 hour period, please contact James O. Wilson, Acting-SPE of 1624 at 571-272-0661. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9306 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0198.

Mark L. Berch
Primary Examiner
Art Unit 1624

June 23, 2004